REMARKS

Claim 7 has been amended for clarification and to insert the limitations of claim 10. This amendment renders claim 9 meaningless and claim 10 redundant, so these claims have been canceled.

Claim 20 has been amended to clarify that cells containing the signal transduction proteins are contacted with the compounds and to delete the word "member" as unnecessary and perhaps confusing. While applicant believes that "the range of organic compounds" is clear, claim 20 has been amended to delete this term. Similarly, the term "marketed" has been deleted.

Claim 22 has been amended to simplify its wording. It will be recalled that claim 22 was grounded in claim 7 as originally presented which simply required that the method be performed in at least two cell types. This wording has been restored in claim 22.

Clearly no new issues are raised and no new matter has been introduced. Thus, entry of the amendment is believed proper.

The Invention

The invention provides a method to obtain a meaningful database that allows the user to ascertain the mode of action of a previously untested compound by analogy to the behavior of known toxins. Because this is made possible, strategies for ameliorating the toxic effect of the newly tested compound can be designed by analogy to those effective against toxins having the greatest similarity in the cellular responses they exhibit. Applicant has recognized that intracellular location patterns of signal transduction factors are significant in analyzing such responses. This is in contrast to others in the art who have focused on the behavior of transcription factors, such as

described in U.S. 5,569,588 and U.S. 5,811,231. Dunlay and Taylor document cited herein focus on transcription factors as well, but understand that translocation is an appropriate readout.

In respect of the present invention method, clearly the more parameters that are meaningful that can be assembled in the database, the more useful the database will be.

Claim 20 describes a method to identify a minimal set of signal transduction proteins that will give the most meaningful results with regard to any compounds to be tested. Essentially, claim 20 describes a method for weeding out signal transduction proteins whose responses to a panel of known toxins are redundant. There is no point in including 10 signal transduction proteins in the database, all of which give the same responses to a set of toxins. As set forth in claim 20, an arbitrary set of signal transduction proteins is first tested for responses to a set of toxins and those whose responses are redundant are discarded, keeping only one representative of each group. Additional proteins are added in a second round of testing and, again, redundant members are discarded. This process is repeated until a set of signal transduction proteins is identified, each of which gives a different response to the set of toxins tested. As required in the conclusion of claim 20, this must result in identification of at least five principal components with respect to the range of compounds that are likely to be tested. That is, redundant signal transduction proteins have been discarded, but there are at least five different patterns available so that across the range of commonly found organic molecules, each of these molecules will provide a response among these components that is characteristic.

The other independent claim, claim 7, is designed to maximize the meaningful information in the database by requiring that the signal transduction protein be assessed at at least three cellular locations. By obtaining this detailed information, greater assurance can be had that pattern

similarity is indicative of similarity of action. As the database will require a multiplicity of signal transduction proteins as defined in claim 20, this requirement has been added to claim 7.

Thus, claim 20 provides a method to obtain the multiplicity of meaningful signal transduction proteins and claim 7 specifies a method to maximize the utility of the database itself.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

The Office asserts that the recitation of "each intracellular localization pattern" is confusing because the referent could be only one localization pattern. Because the method of the invention is maximally useful when multiple intracellular location distributions are employed, the limitations of claim 10 have been inserted. It is believed this obviates the rejection.

The Office also objects to the recitation of "optionally as a function of time." Although applicant does not understand the rationale for this objection, this phrase has been canceled. It was inserted merely as antecedent basis to the limitation of claim 21. As claim 21 recites "further including" this step, it is believed unnecessary to include this phrase in claim 7.

The Office also objects to the term "arbitrarily" in claim 20. Respectfully, applicant believes this term is clear. There are no degrees of arbitrariness. Arbitrary is arbitrary. As long as the first set contains signal transduction proteins, it does not matter what they are. It will be clear to the practitioner that "arbitrarily" simply means that there is no particular basis to pick one signal transduction protein over another.

The Office further objects to the recitation of "significant." Respectfully, it is believed this term is well understood and is used all the time. Here, it simply means that the pattern changes are detectable in a reliable way above background.

It is believed the amendment to claim 20 clarifies the step of "contacting" and obviates the objection to the phraseology "each member."

With respect to the objection to "adding new signal transduction proteins," applicant could add additional verbiage, but believes that it would merely muddy the waters. The section referred to in the claim could be amended to read:

> discarding those signal transduction proteins from said first set whose changes in intracellularly localization pattern are redundant to obtain a first set with a reduced number of signal transduction proteins;
>
> adding new signal transduction proteins to said first set with a reduced number of signal transduction proteins to provide a second set of signal transduction proteins; etc.

While it is made explicit what the second set is added to, the excess verbiage seems unnecessary to understand what is being claimed.

As to the next objection to repeating the steps for which the second set of signal transduction proteins was used, this is necessary because it may not be possible with only two iterations to obtain sufficient information to provide a meaningful database.

As to the objection to the term "marketed," the intent is simply to make the database of practical scope rather than attempting to include exotic compounds that may not be of interest; however, this terms has been deleted as unnecessary, as has "range."

As to the last objection, again, perhaps explicitness has been sacrificed for conciseness. It is the data with regard to the signal protein that are discarded.

The Rejection Under 35 U.S.C. § 102

Claims 7, 9-10, 12-13 and 20-22 were rejected as assertedly anticipated by Dunlay and Taylor (U.S. 5,989,835).

First, with respect to claim 20, applicant is unable to find anything resembling the steps set forth in claim 20 in Dunlay and Taylor. Respectfully, the inclusion of claim 20 in this basis for rejection appears to be in error.

With respect to claim 7 and its dependent claims, applicant acknowledges that Dunlay and Taylor is relevant in that a database is obtained with respect to the effect of a set of compounds on the location of various cellular moieties within cells. However, of course, in order for anticipation to be found, each and every limitation of the claim must be met by the cited document. There are at least two limitations of claim 7 that are not disclosed by Dunlay and Taylor. The first is that there is no requirement in Dunlay and Taylor that all of the compounds in the set be toxic compounds. While some of the compounds tested may incidentally be toxic, this is not the same thing as providing "a set of toxic compounds."

More importantly, there is no disclosure in Dunlay and Taylor that the intracellular localization pattern be constructed by concurrently assessing the signal transduction protein at at least three cellular locations as specified in claim 7. The Office disputes this, citing column 11, lines 23-46. However, this section does not support the conclusion drawn that the location of a signal transduction protein at three cellular locations is described. This section describes only translocation between the cytoplasm and the plasma membrane. The examples each only describe locating a single protein in the nucleus or the cytoplasm. In no case is there a description of locating a single protein in at least three cellular locations.

This distinction is important because the database is more useful if it includes more information on responses from the toxins selected for inclusion in it. The more parameters measured, the more likely that an independent toxin will indeed generate a discernible response.

In sum, two essential limitations of claim 7 are not disclosed in Dunlay and Taylor. The first is that Dunlay and Taylor do not describe using, specifically, a set of toxic compounds and describe the determination of cellular localization with respect to a single protein only with respect to two cellular locations, which is insufficient to provide as meaningful a database as that obtainable by the method of the present claims.

For this reason, the rejection for anticipation may properly be withdrawn.

The Rejection Under 35 U.S.C. § 103

Claims 8 and 11 were rejected over the combination of Dunlay and Taylor with additional documents – in the case of claim 8, Mochly-Rosen, *Science* (1995) 268:247 and in the case of claim 11, Gerhard (U.S. 5,684,628). These rejections are traversed for the same reasons set forth above. Dunlay and Taylor fail to teach essential elements of the invention, and thus fail to anticipate or to suggest the invention as claimed. The combination of Dunlay and Taylor with the secondary documents appears taught by the invention itself, rather than suggested by the art.

Claim 20 was rejected as obvious over the combination of Dunlay and Taylor with Cook (U.S. 6,546,378). However, as noted above, there is no disclosure whatsoever in Dunlay and Taylor of the method of claim 20 and so its combination with Cook cannot yield or suggest the invention as claimed. The mere mention of principal component analysis in column 19 of Cook appears unrelated to anything described in Dunlay and Taylor in any case. Principal component analysis is simply a known method of grouping parameters that show similar responses as indeed required by claim 20. Thus, if signal transduction protein A and signal transduction protein B give the same response pattern to the panel of toxins, either one of them can be used as a "principal component" to

assess a response. There is nothing contributed by Cook to this concept. Accordingly, this basis for rejection may also be withdrawn.

Request for Withdrawal of Finality

Applicant respectfully requests the Office to reconsider the finality of the present Office action. While the claims were amended in response to the previous Office action, it is not seen how the amendment necessitated the new grounds for rejection. An entirely different document has been cited which was as applicable to the claims as previously worded as it is to those now pending. The essential features of claim 7 – *i.e.*, method to obtain a database by looking at the cellular locations of proteins in response to toxins, existed in claim 7 as previously pending. The modification of this claim to add the requirement for three intracellular locations to be assessed does not necessitate citation of, but distinguishes Dunlay and Taylor. As noted previously, Dunlay and Taylor is inapplicable to claim 20 as amended, so this amendment cannot be considered to compel citation of this document. Applicant would be grateful for reconsideration of finality in view of the relevance of Dunlay and Taylor to the claim 7 as previously drawn.

Conclusion

Claim 20 appears free of the art as the iterative process described in claim 20 is nowhere suggested in any of the cited documents. It is believed that the rejections of various portions of claim 20 for indefiniteness have been obviated by amendment or discussion. Accordingly, claim 20 should be in a position for immediate allowance.

As to claim 7 and its dependent claims, Dunlay and Taylor fail to suggest at least two essential limitations of claim 7 and, indeed, the focus of Dunlay and Taylor is elsewhere. The focus is on transcription factors and their location in the cytoplasm or nucleus rather than signal

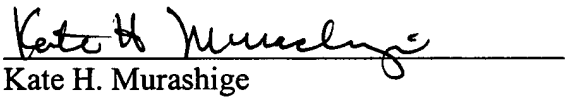
transduction proteins and their intracellular localization, despite a casual mention in the concluding paragraphs of translocation other than simply from the cytoplasm to the nucleus. It is only the invention that recognizes the importance of intracellular localization patterns in ascertaining the effect of toxins and the importance of databases for associating the behavior of unknown compounds with the behavior of known toxins so that advantage could be taken of the knowledge related to such known toxins in addressing the effects of compounds whose behavior has not yet been tested.

Thus, applicant believes that as well as claim 20, claim 7 and its dependent claims, claims 8, 11-13 and 21-22, are in a position for allowance.

If minor issues remain that could be resolved by telephone, a phone call to the undersigned is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 388512010411.

Respectfully submitted,

Dated: June 28, 2005 By: 

Kate H. Murashige
Registration No. 29,959
MORRISON & FOERSTER LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130-2332
Telephone: (858) 720-5112
Facsimile: (858) 720-5125